

83. (Amended) The [milk] method of claim 82, wherein the human polypeptide is lactoferrin.

98. (Amended) The method of claim 125, wherein the promoter is [A transgenic bovine having a genome containing a transgene comprising:]

a bovine  $\alpha$ -s1 casein promoter; and the enhancer is a  
a bovine  $\alpha$ -s1 casein enhancer[;

a secretory DNA sequence encoding a signal sequence functional in bovine mammary secretory cells;

a recombinant DNA sequence encoding a recombinant polypeptide, the secretory DNA sequence being operably linked to the recombinant DNA sequence, wherein a secretory recombinant DNA sequence is formed, the secretory-recombinant DNA sequence being operably linked to the bovine  $\alpha$ -s1 promoter and enhancer;

wherein the transgene, in a lactating form of the bovine or a female descendant of the bovine, is capable of directing the expression of the secretory-recombinant DNA sequence in bovine mammary secretory cells to produce a form of recombinant polypeptide, that when secreted from the mammary secretory cells produces the recombinant polypeptide in the milk of the bovine or female descendant thereof].

99. (Amended) The [transgenic bovine] method of claim 98, wherein the transgene further comprises:

an  $\alpha$ -s1 casein 3' untranslated sequence.

100. (Amended) The [transgenic bovine] method of claim 99, wherein the transgene further comprises an  $\alpha$ -s1 casein 3' flanking sequence.

101. (Amended) The [transgenic bovine] method of claim 100, wherein the  $\alpha$ -s1 casein 3' flanking sequence has a length of at least 2 kb.

102. (Amended) The [transgenic bovine] method of claim 101, wherein the transgene further comprises at least 16 kb of  $\alpha$ -s1 casein 5' flanking sequence.

103. (Amended) The [transgenic bovine] method of claim 102, wherein the transgene further comprises an intronic sequence.

104. (Amended) The [transgenic bovine] method of claim 103, wherein the intronic sequence is a hybrid intronic sequence.

105. (Amended) The [transgenic bovine] method of claim 104, wherein the hybrid intronic sequence comprises a 5' portion of a bovine  $\alpha$ -S1 casein intronic sequence and a 3' portion of an IgG heavy chain intronic sequence.

106. (Amended) The [transgenic bovine] method of claim 105 wherein the 3' portion is a 3' splice signal sequence associated with the J-C segment rearrangement of an IgG heavy chain.

107. (Amended) The [transgenic bovine] method of claim 106, wherein the recombinant polypeptide is a homologous polypeptide from the bovine.

108. (Amended) The [transgenic bovine] method of claim 106, wherein the recombinant polypeptide is a heterologous polypeptide.

109. (Amended) The [transgenic bovine] method of claim 108, wherein the heterologous polypeptide is selected from the group consisting of human milk proteins, human serum proteins, and industrial enzymes.

110. (Amended) The [transgenic bovine] method of claim 109, wherein the heterologous polypeptide is a human milk protein.

111. (Amended) The [transgenic bovine] method of claim 110, wherein the human milk protein is selected from the group consisting of secretory immunoglobulins, lysozyme, lactoferrin, lactoglobulin,  $\alpha$ -lactalbumin and bile salt-stimulated lipase.

112. (Amended) The [transgenic bovine] method of claim 111, wherein the milk protein is lactoferrin or lysozyme.

113. (Amended) The [transgenic bovine] method of claim 108, wherein the heterologous polypeptide is a human serum protein.

114. (Amended) The [transgenic bovine] method of claim 113, wherein the human serum protein is selected from the group consisting of albumin, immunoglobulin, Factor VIII, Factor IX and Protein C.

115. (Amended) The [transgenic bovine] method of claim 114, wherein the serum protein is albumin.

116. (Amended) The [transgenic bovine] method of claim 108, wherein the heterologous polypeptide is an industrial enzyme selected from the group consisting of proteases, lipases, chitinases and ligninases.

117. (Amended) The [transgenic bovine] method of claim 106, wherein the recombinant polypeptide is a naturally occurring polypeptide.

118. (Amended) The [transgenic bovine] method of claim 98, wherein the transgene is the 26 kb NotI fragment of plasmid p26,8h1F4.

123. (Amended) A method of producing a transgenic bovine species the method comprising:

obtaining an ovum from bovine ovaries;  
maturing and fertilizing the ovum *in vitro* to form a zygote;  
introducing a transgene into the zygote *in vitro*;  
propagating the zygote to form the embryo *in vitro*; and  
transplanting the embryo into a recipient female bovine parent, which gestates the embryo to give birth to a transgenic bovine.

125. (Amended) [A transgenic bovine produced by] [t]The method of claim 123 wherein the transgene comprises [having a genome containing a transgene comprising]:

a mammary-gland specific promoter;

a mammary-gland specific enhancer;  
a secretory DNA sequence encoding a signal sequence functional in bovine mammary secretory cells;

a recombinant DNA sequence encoding a recombinant polypeptide, the secretory DNA sequence being operably linked to the recombinant DNA sequence, wherein a secretory recombinant DNA sequence is formed, the secretory-recombinant DNA sequence being operably linked to the promoter and enhancer;

wherein the transgene, in a lactating form of the transgenic bovine or a female descendent of the transgenic bovine, is capable of directing the expression of the secretory-recombinant DNA sequence in bovine mammary secretory cells to produce a form of recombinant polypeptide, that when secreted from the mammary secretory cells produces the recombinant polypeptide in the milk of the bovine or female descendent thereof.

126. (Amended) The [transgenic bovine] method of claim [124] 123, wherein the transgene is introduced into the zygote by microinjection.

Please add the following claim.

128. A method of producing an embryo of a transgenic bovine species, comprising:

obtaining an ovum from bovine ovaries;  
maturing and fertilizing the ovum *in vitro* to form a zygote;

introducing a transgene into the zygote, wherein the transgene integrates into the genome of the zygote to form the transgenic embryo.

#### Remarks

##### Preliminary

With the exception of new claim 128, all claims are now dependent directly or indirectly on claim 123. Claim 123 is direct to an *in vitro* method of producing a transgenic bovine species. The claim specifies that steps of maturing an oocyte, fertilizing the oocyte to produce a zygote, introducing a transgene into the zygote and maturing the zygote to an embryo are conducted *in vitro*. Support for the step of maturing an